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Evidence Synthesis: Navigating an Evolving Landscape

Reflections from the NIHR Complex Reviews Support Unit

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Acknowledgement: Ellesha Smith for help with slides

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My Background

- Statistician
- 25 years research experience (nearly exclusively!) in methodological and applied evidence synthesis

Aims of Talk

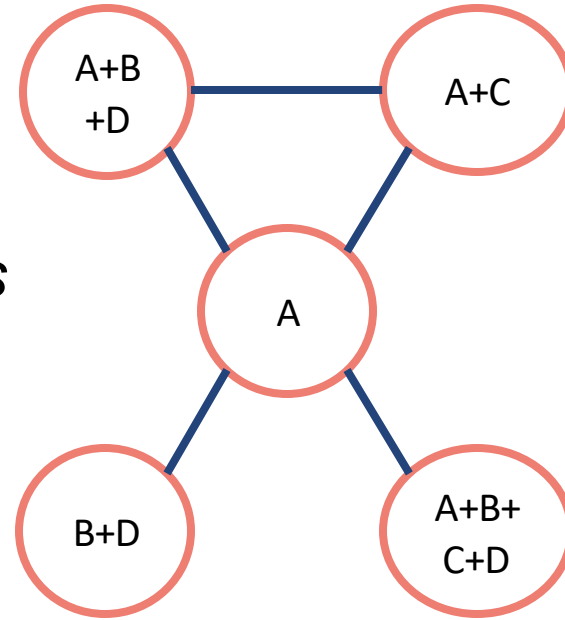
- Highlight 2 particularly interesting, complex & challenging reviews CRSU collaborated on
 - Indication of what is possible / desirable(?) at the methodological “cutting-edge” using emerging methodology
- Outline CRSU developed software
 - Designed to aid others doing complex data synthesis

Case Study 1

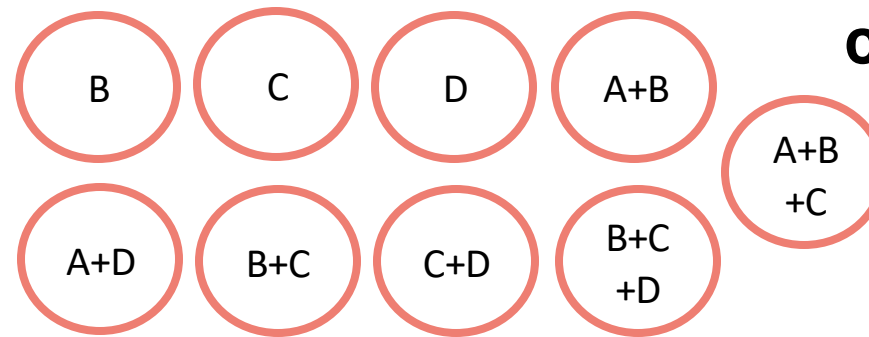
Component Network Meta-Analysis: Behavioural interventions for smoking cessation

What is component network meta-analysis?

Component combinations evaluated in studies:



CNMA can also estimate effects of:



- Component network meta-analysis can evaluate the effectiveness of components and *every* combination of components, **including combinations not compared in studies**

Behavioural interventions for smoking cessation: an overview and network meta-analysis

✉ [Jamie Hartmann-Boyce](#), [Jonathan Livingstone-Banks](#), [José M Ordóñez-Mena](#), [Thomas R Fanshawe](#), [Nicola Lindson](#), [Suzanne C Freeman](#), [Alex J Sutton](#), [Annika Theodoulou](#), [Paul Aveyard](#) [Authors' declarations of interest](#)

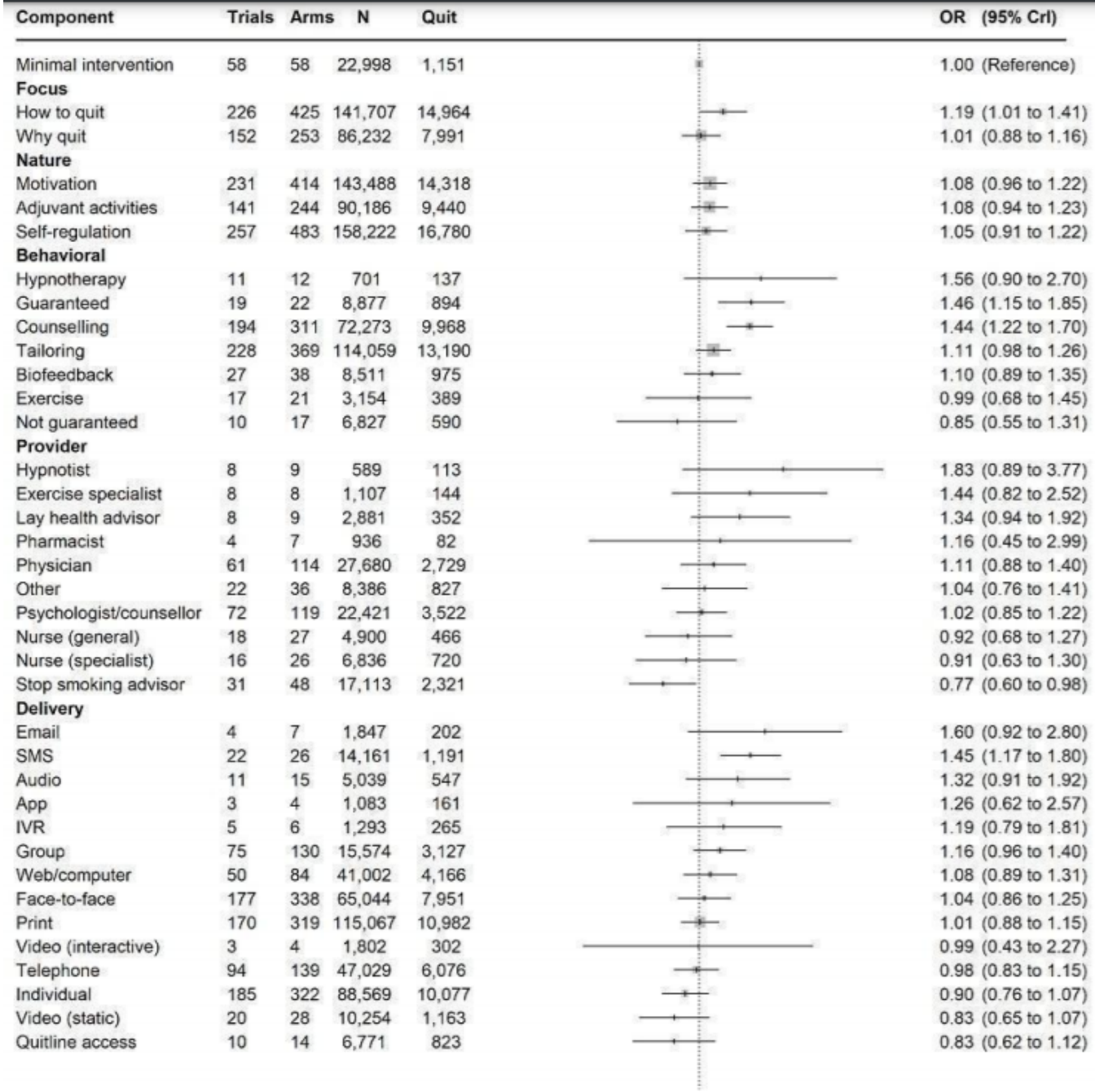
Version published: 04 January 2021 [Version history](#)

<https://doi.org/10.1002/14651858.CD013229.pub2> [↗](#)

- Objective: conduct a component network meta-analysis to determine how modes of delivery; person delivering the intervention; and the nature, focus, and intensity of behavioural interventions for smoking cessation influence the likelihood of achieving abstinence six months after attempting to stop smoking; and whether the effects of behavioural interventions depend upon other characteristics, including population, setting, and the provision of pharmacotherapy.

Evidence Base

- 33 previous Cochrane reviews used to identify studies:
 - From which 312 randomised controlled trials, representing 250,563 participants and 845 distinct study arms, met the criteria for inclusion in the component network meta-analysis.
 - 38 different components identified
 - This represented 437 different combinations of components(!)



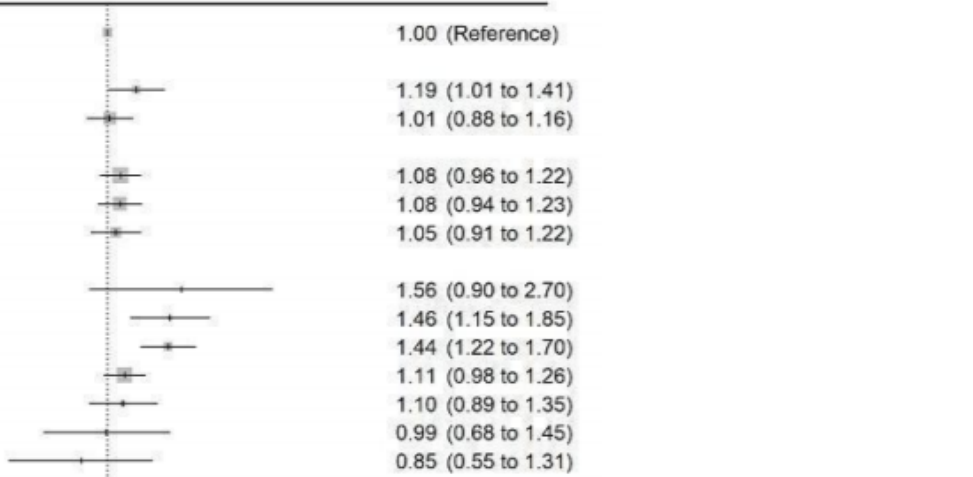
Results:

Summary forest plot showing effect estimates for each component as related to smoking cessation

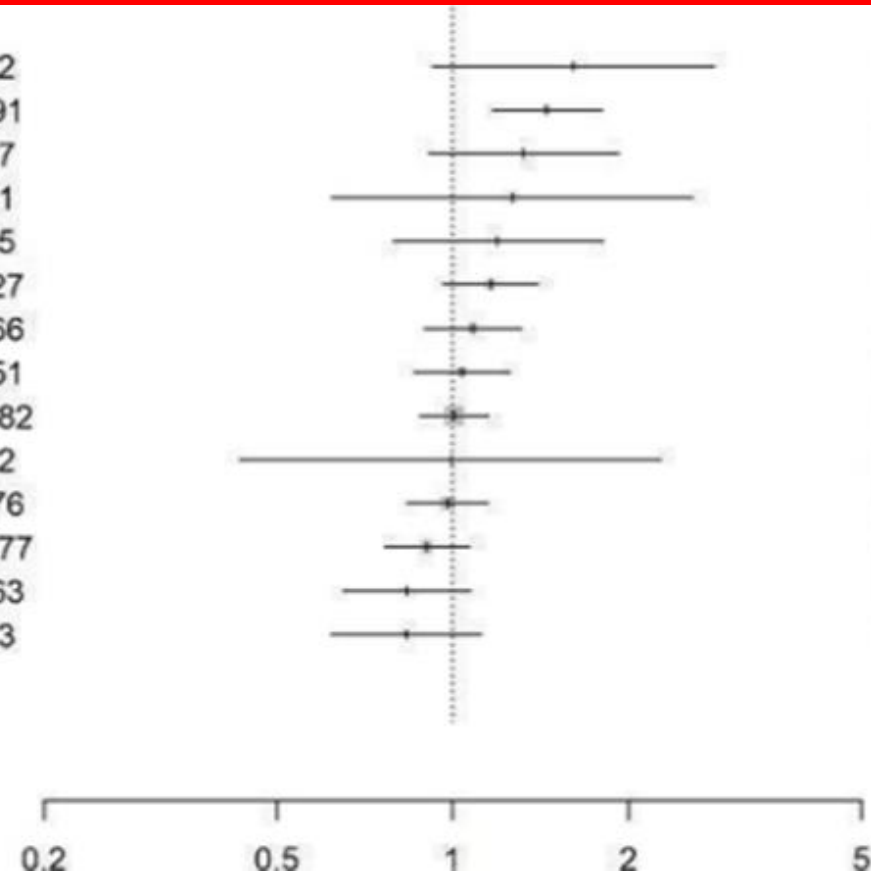
Results:

Summary forest plot showing effect estimates for each component as related to smoking cessation

Component	Trials	Arms	N	Quit	OR (95% CrI)
Minimal intervention	58	58	22,998	1,151	1.00 (Reference)
Focus					
How to quit	226	425	141,707	14,964	1.19 (1.01 to 1.41)
Why quit	152	253	86,232	7,991	1.01 (0.88 to 1.16)
Nature					
Motivation	231	414	143,488	14,318	1.08 (0.96 to 1.22)
Adjuvant activities	141	244	90,186	9,440	1.08 (0.94 to 1.23)
Self-regulation	257	483	158,222	16,780	1.05 (0.91 to 1.22)
Behavioral					
Hypnotherapy	11	12	701	137	1.56 (0.90 to 2.70)
Guaranteed	19	22	8,877	894	1.46 (1.15 to 1.85)
Counselling	194	311	72,273	9,968	1.44 (1.22 to 1.70)
Tailoring	228	369	114,059	13,190	1.11 (0.98 to 1.26)
Biofeedback	27	38	8,511	975	1.10 (0.89 to 1.35)
Exercise	17	21	3,154	389	0.99 (0.68 to 1.45)
Not guaranteed	10	17	6,827	590	0.85 (0.55 to 1.31)

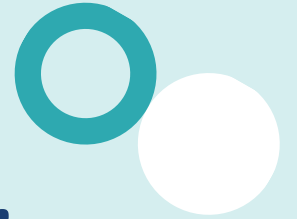


Delivery	Trials	Arms	N	Quit	OR (95% CrI)
Email	4	7	1,847	202	1.60 (0.92 to 2.80)
SMS	22	26	14,161	1,191	1.45 (1.17 to 1.80)
Audio	11	15	5,039	547	1.32 (0.91 to 1.92)
App	3	4	1,083	161	1.26 (0.62 to 2.57)
IVR	5	6	1,293	265	1.19 (0.79 to 1.81)
Group	75	130	15,574	3,127	1.16 (0.96 to 1.40)
Web/computer	50	84	41,002	4,166	1.08 (0.89 to 1.31)
Face-to-face	177	338	65,044	7,951	1.04 (0.86 to 1.25)
Print	170	319	115,067	10,982	1.01 (0.88 to 1.15)
Video (interactive)	3	4	1,802	302	0.99 (0.43 to 2.27)
Telephone	94	139	47,029	6,076	0.98 (0.83 to 1.15)
Individual	185	322	88,569	10,077	0.90 (0.76 to 1.07)
Video (static)	20	28	10,254	1,163	0.83 (0.65 to 1.07)
Quitline access	10	14	6,771	823	0.83 (0.62 to 1.12)



Case Study 2

Enamel caries detection and diagnosis: Network meta-analysis of diagnostic test accuracy (DTA) studies



Enamel Caries Detection and Diagnosis: An Analysis of Systematic Reviews

T. Walsh¹ , R. Macey¹, D. Ricketts², A. Carrasco Labra^{3,4},
H. Worthington¹, A.J. Sutton⁵, S. Freeman⁵ , A.M. Glenny¹,
P. Riley¹, J. Clarkson^{1,2}, and E. Cerullo⁵

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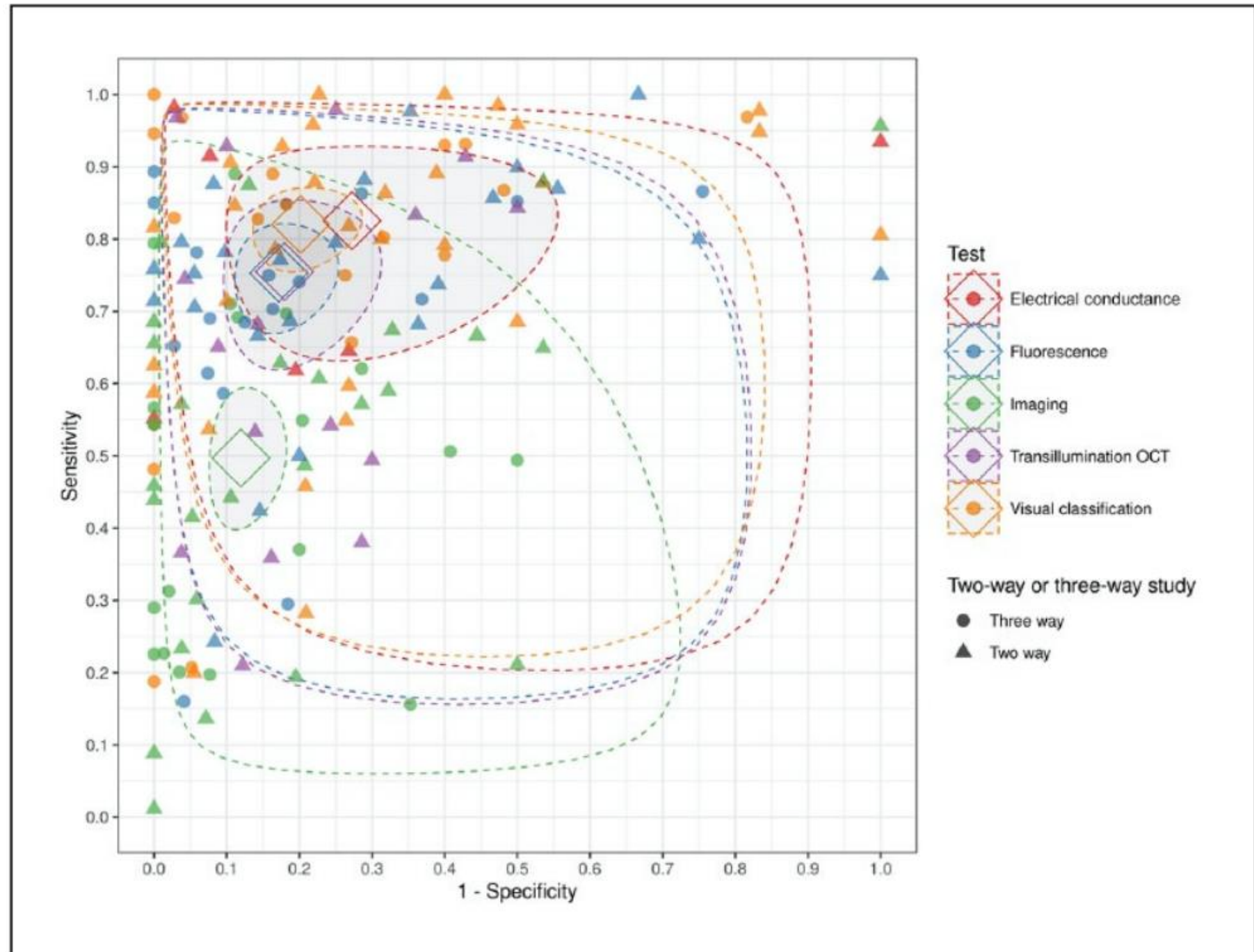
DOI: 10.1177/00220345211042795

journals.sagepub.com/home/jdr

- Aim: Undertake a formal comparative analysis of the diagnostic accuracy of 5 technologies to provide a firm foundation on which to base clinical decision making, clinical guidelines, and policy.
- Review group had just completed 5 Cochrane DTA reviews of individual technologies to detect caries
- This was the comparative network analysis using evidence from the 5 reviews

Results

- ROC plot of comparative analysis of the 5 technologies



Take Home Messages

- Analyses aim to answer very relevant clinical questions usually beyond the scope of individual studies
 - E.g. Which components/tests work best?
- Moving towards summarising whole research fields
- Extending “standard” network meta-analysis

The CRSU online “Apps”

<http://www.nihrcrsu.org/guidance/apps>

Or Google “CRSU apps”

BACKGROUND

Aims of the CRSU

- Provide flexible, timely and appropriate response to specific requests, to support successful delivery of the complex reviews
- Contribute to building capacity and capability within the research community

Challenge

- Often reviews don't have experienced statistical support

BACKGROUND (cont.)

- Identified two barriers:
 - Lack of awareness more sophisticated / appropriate synthesis methods existed
 - But that's a different talk
 - Lack of statistical software expertise to implement methods

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Solution: Create user-friendly software for the non-expert



THE CRSU APPS

(<http://www.nihrcrsu.org/guidance/apps/>)

- **MetaInsight:** Conducts Network Meta-Analysis
- **MetaDTA:** Conducts Meta-Analysis of Diagnostic Test Accuracy Studies
- **MetaInsight:Covid-19:** Proof of concept - tool for exploration, re-analysis, sensitivity analysis, and interrogation of published meta-analysis. Shadowed a living systematic review of Covid treatments
- **DTA primer:** Interactive explorable explanation is designed to teach the basics of diagnostic test accuracy evaluation

You have selected **Continuous** outcome on the 'Home' page. The analysis page for **Continuous** outcomes are now displayed.

Data table (Click to open / hide this panel)

- 1. Data summary
- 2. Frequentist network meta-analysis**
- 3. Bayesian network meta-analysis

- 2a. Forest Plot**
- 2b. Comparison of all treatment pairs
- 2c. Inconsistency

Outcome for continuous data:

- Mean Difference (MD)
- Standardised Mean Difference (SMD)

For treatment rankings, smaller outcome values (e.g. smaller mean values for continuous data, or ORs less than 1 for binary data) are:

- Desirable
- Undesirable

Model:

- Random effect (RE)
- Fixed effect (FE)

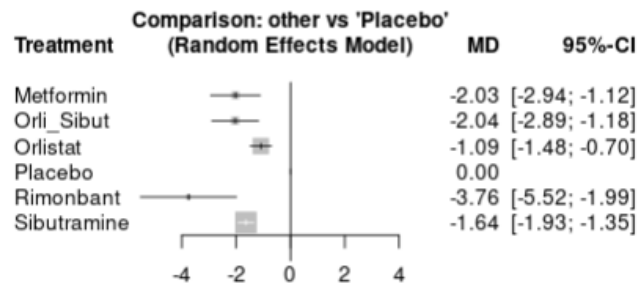
Select studies to exclude:

Tips: you can use the data table to help find the study that you want to exclude.

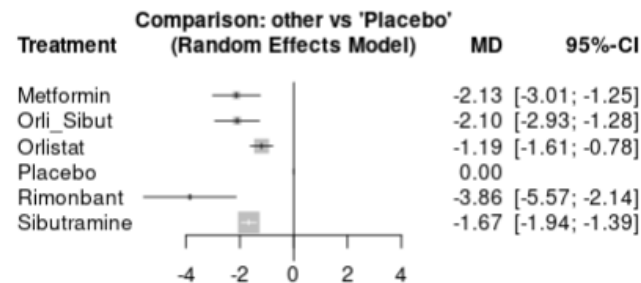
Open the data table

- Kuo 2006
- Ozcelik 2004
- Turker 2006
- Wang 2005
- Schechter 2006
- Aydin 2004

Results for all studies



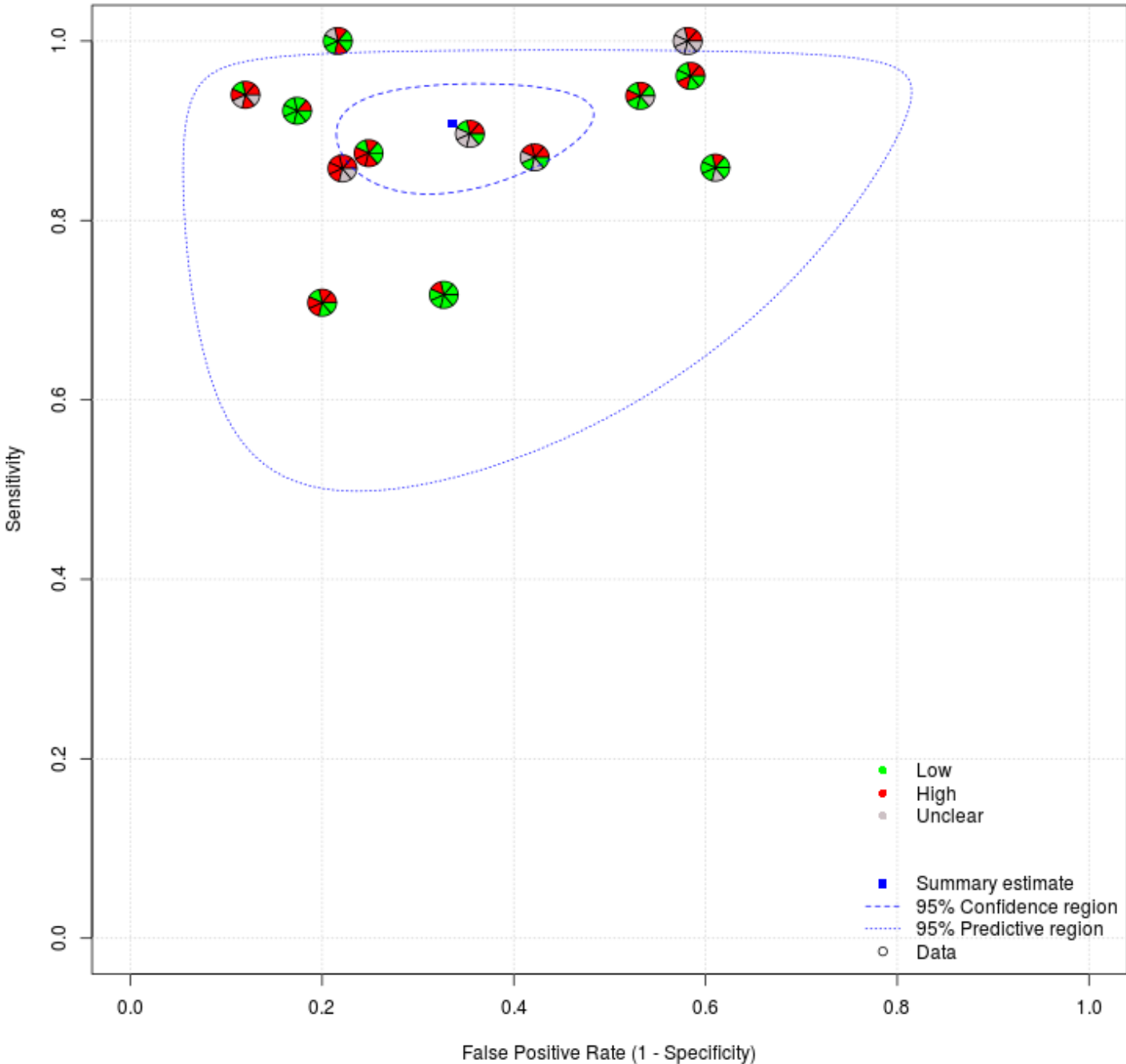
Results with studies excluded



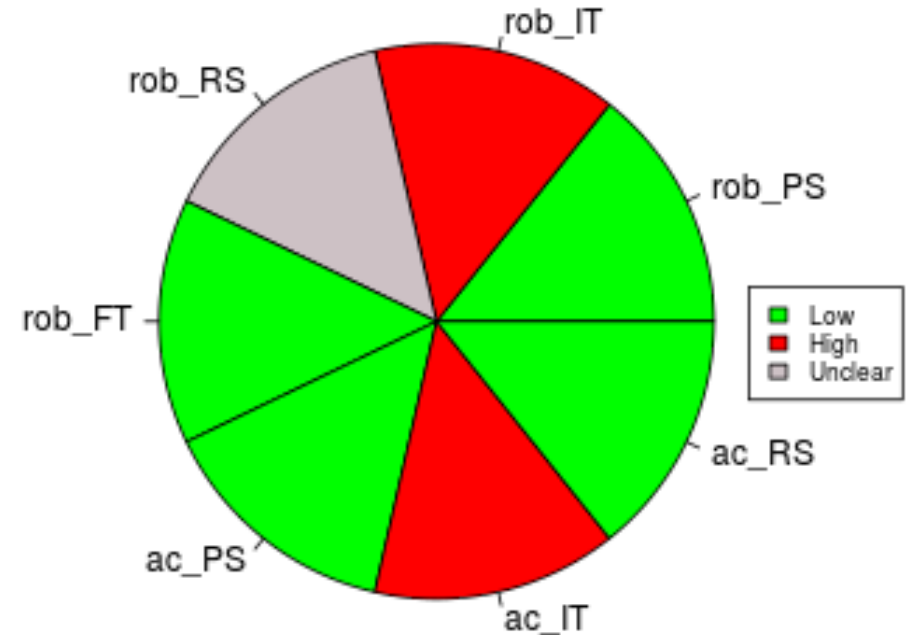
Between-study standard deviation: 0.41 , Number of studies: 24 ,
 Number of treatments: 6
 All outcomes are versus the reference treatment: Placebo

Between-study standard deviation: 0.37 , Number of studies: 22 ,
 Number of treatments: 6

Random Effects Meta-Analysis



Scores from each element of the QUADAS-2 tool



Patel A, Cooper NJ, Freeman SC, Sutton AJ. Graphical enhancements to summary receiver operating characteristic plots to facilitate the analysis and reporting of meta-analysis of diagnostic test accuracy data. *Research Synthesis Methods* 2020, <https://doi.org/10.1002/jrsm.1439>.

Usage & Future

- Apps get used worldwide for approx. 800 hours a month total (mostly MetaInsight and MetaDTA)
- MetaInsight paper cited approx. 50 times since published in 2019
- MetaDTA paper cited 80+ times since published in 2019
- NIHR funding until November 2023 for apps (only)
- New features in development.....

THANK YOU

<http://www.nihrcrsu.org/guidance/apps>

Or Google “CRSU apps”